

(FILE 'HOME' ENTERED AT 08:05:24 ON 19 MAR 1999)

FILE 'USPATFULL' ENTERED AT 08:05:32 ON 19 MAR 1999

FILE 'MEDLINE, EMBASE, CAPLUS' ENTERED AT 08:05:53 ON 19 MAR 1999

L1 1276 S MESODERM? AND (BMP? OR HEDGEHOG OR WNT? OR VEGF?)

L2 97 S L1 AND (HEMATOP? OR HEMATAO? OR HEAMATOP? OR VASCUL?)

FILE 'MEDLINE' ENTERED AT 08:16:10 ON 19 MAR 1999

FILE 'MEDLINE, EMBASE, CAPLUS' ENTERED AT 08:19:19 ON 19 MAR 1999

L3 52 S L2 NOT PY>1997

L4 24 DUP REM L3 (28 DUPLICATES REMOVED)
E BARON M/AU

L5 129 S E9

E FARRINGTON S/AU

L6 25 S E5-E7

E BARON MARG/AU

L7 26 S E5

E BELAOUSOFF/AU

L8 9 S E4-E5

L9 170 S L5 OR L6 OR L7 OR L8

E HEMATO?/

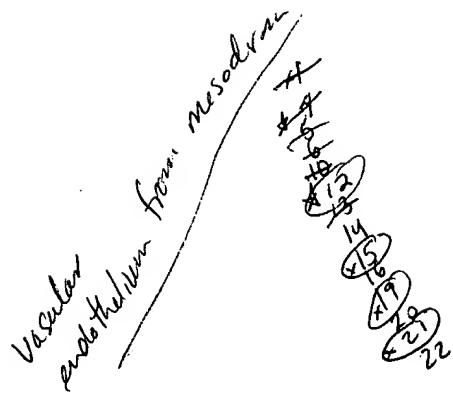
L10 9 S L9 AND (HEMATOP? OR HEAMATOP? OR HEMATAO? OR VASCUL?)

L11 7 DUP REM L10 (2 DUPLICATES REMOVED)

(FILE 'USPAT' ENTERED AT 15:25:13 ON 18 MAR 1999)

L1 1013 S BMP? OR HEDGEHOG OR WNT?
E HEMAT/
E HEAMAT/
L2 3289 S E14 OR E15 OR HEMATAOPO? OR HEMATOPO?
L3 103 S L1 AND L2
L4 3 S L1(15A) (VASCUL?)
L5 77 S L3 AND (EMBRYO? OR MESODERM? OR UNDIFFERENT?)

Novel



L4 ANSWER 19 OF 24 LINE

PLICATE 12

TI The angiogenic potentials of the cephalic **mesoderm** and the origin of brain and head blood vessels.

AU Couly G; Coltey P; Eichmann A; Le Douarin N M

SO MECHANISMS OF DEVELOPMENT, (1995 Sep) 53 (1) 97-112.

Journal code: AXF. ISSN: 0925-4773.

AB We have used two molecular markers to label blood vessel endothelial cells

and their precursors in the early avian embryo. One marker, called Quek1, is the avian homologue of the mammalian VEGF receptor flk-1 and the other is the MB1/QH1 monoclonal antibody. Quek1 is expressed in a subset of **mesodermal** cells from the gastrulation stage. Quek1 positive cells later form blood vessel endothelial cells and express the MB1/QH1 antigen which is specific for endothelial and hemopoietic cells

of the quail species. These two markers allowed us first to show that the cephalic paraxial **mesoderm** has angiogenic potentials which are much more extended than its trunk counterpart (the somites). Secondly, the

origin of the endothelial cells lining the craniofacial and head blood vessels was mapped on the 3-somite stage cephalic **mesoderm** via the quail-chick chimera technique, in which well defined **mesodermal** territories are exchanged between stage-matched embryos of both species in a strictly isotopic manner. We found that the anterior region of the cephalic paraxial **mesoderm** is largely recruited to provide the forebrain and the upper face with their **vasculature**. This means that large volumes of tissues are **vascularized** by a discrete region of the cephalic **mesoderm**, the fate of which is otherwise to give rise to muscles. The widespread expansion of the angiogenic cells arising from the anterior paraxial **mesoderm** must be related to the high growth rate of the anterior region of the neural primordium, yielding the telencephalon and of the neural crest-derived facial structures which are themselves devoid of angiogenic

ANSWER 5 OF 24 CAPLUS COPYRIGHT 1999 ACS

TI Development and differentiation of blood vessels in the central nervous system

AU Wilting, J.

SO Neuroendocrinol., [Ernst Berta Scharrer Symp.] (1997), 305-312.

Editor(s): Korf, Horst-Werner; Usadel, Klaus-Henning. Publisher:

Springer,

Berlin, Germany.

CODEN: 66EOAA

AB A review, with 44 refs. The central nervous system (CNS) develops from a pseudostratified ectodermal epithelium contg. neuroblasts and glioblasts. Other constituents (microglia, blood vessels) are of **mesodermal** origin and successively invade the neuroectoderm. Using chick-quail chimeras it is possible to study the interaction between neuroectodermal and **mesodermal** cells. **Vascular** endothelial cells start invading the CNS of birds at about day 3.5 of development. They originate from the paraxial **mesoderm** of the head and the trunk. Thereafter, smooth muscle cells migrate along the endothelial routes. Neuroectodermal cells secrete **vascular** endothelial growth factor (VEGF), which is a highly specific angiogenic and chemoattractive factor. Angioblast and endothelial cells in the paraxial **mesoderm** are characterized by the expression of VEGF -receptor-2. Except for the choroid plexus, VEGF and VEGF receptors are not expressed in the adult brain. The organ-typical differentiation of endothelial cells in the CNS depends on interactions with local neuroectodermal cells. Development of blood-brain

barrier characteristics are obviously due to inductive signals from astrocytes. In contrast, the epithelial cells of the choroid plexus induce development of highly permeable, fenestrated capillaries. Constitutive expression of VEGF and its receptors in the choroid plexus (and the kidney glomeruli) may serve as the basis for high permeability. VEGF has been shown to increase **vascular** permea

4 MEDLINE

DUPLICATE 13

TI **Vascularization** of the mouse embryo: a study of flk-1, tek, tie, and **vascular** endothelial growth factor expression during development.

AU Dumont D J; Fong G H; Puri M C; Gradwohl G; Alitalo K; Breitman M L

SO DEVELOPMENTAL DYNAMICS, (1995 May) 203 (1) 80-92.

Journal code: A9U. ISSN: 1058-8388.

AB We report the detailed developmental expression profiles of three endothelial specific receptor tyrosine kinases (RTKs) flk-1, tek, tie, as well as **vascular** endothelial growth factor (**VEGF**), the flk-1 ligand. We also examined the expression of the other **VEGF** receptor, flt-1, during placental development. flk-1, tek, and tie transcripts were detected sequentially at one-half day intervals starting at E7.0, suggesting that each of these RTKs play a unique role during **vascularization** of the mouse embryo. All three RTKs were expressed in the extraembryonic and embryonic **mesoderm** in regions that eventually give rise to the **vasculature**. Except for the expression of tek and flk-1 in the **mesoderm** of the amnion, the expression of these RTKs from E8.5 onwards was virtually indistinguishable. An abundant amount of flt-1 transcripts was found in the spongiotrophoblast cells of the developing placenta from E8.0 onwards.

This cellular compartment is located between the maternal and labyrinthine layers of the placenta, which both express **VEGF**. **VEGF** transcripts were detected as early as E7.0 in the endoderm juxtaposed to the flk-1 positive **mesoderm**, and later in development **VEGF** expression displayed an expression profile both contiguous with that of flk-1, and also in tissues found some distance from the flk-1-expressing endothelium. These results suggest a possible dual role for **VEGF** which includes a chemotactic and/or a cellular maintenance role for **VEGF** during **vascularization** of the mouse emb

L4 ANSWER 14 OF 24 MEDLINE

DUPPLICATE 8

TI In vitro analysis of epiblast tissue potency for **hematopoietic** cell differentiation.

AU Kanatsu M; Nishikawa S I

SO DEVELOPMENT, (1996 Mar) 122 (3) 823-30.

Journal code: ECW. ISSN: 0950-1991.

AB In murine embryogenesis, all cells that will constitute the embryonic structures originate from the epiblast (primitive ectoderm) tissue, the epithelial cell sheet of the gastrulating embryo. The cells of this tissue

are totipotent at the beginning of gastrulation, but at the end of this period are specified to particular cell lineages. Thus, it is likely that during murine gastrulation, the potency of epiblast cells that were originally totipotent becomes restricted as development progresses. However, the mechanisms of this process are unknown. We have investigated this process *in vitro*, focusing on the **hematopoietic** cell lineage. To detect the hematogenic potency of the epiblast tissue, we established an *in vitro* culture system in which the **hematopoietic** cell differentiation of the epiblast tissue was supported by a stromal cell layer. With this culture system, we investigated the process by

which

this potency becomes spatially and temporally restricted during gastrulation. The results showed that hematogenic potency resides in the entire epiblast of the early- to mid-gastrulating embryo, but becomes restricted to the posterior half of the epiblast at the headfold stage. Furthermore, we showed that this process is altered by exogenous bone morphogenetic protein-4 (**BMP-4**) or activin A, which may be **mesoderm** inducers in *Xenopus* embryogenesis.

L11 ANSWER 1 OF 7 CAPLUS COPYRIGHT 1999 ACS
TI Embryonic induction of **hematopoietic** and **vascular**
mesoderm in the developing mouse
AU **Belaoussoff, Maria**
SO (1998) 211 pp. Avail.: UMI, Order No. DA9832323
From: Diss. Abstr. Int., B 1998, 59(5), 2017

L11 ANSWER 2 OF 7 CAPLUS COPYRIGHT 1999 ACS
TI Methods for modulating **hematopoiesis** and **vascular**
growth
IN **Baron, Margaret H.; Farrington, Sarah M.;**
Belaoussoff, Maria
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2

L11 ANSWER 3 OF 7 MEDLINE DUPLICATE 1
TI **Hematopoietic** induction and respecification of A-P identity by
visceral endoderm signaling in the mouse embryo.
AU **Belaoussoff M; Farrington S M; Baron M H**
SO DEVELOPMENT, (1998 Dec) 125 (24) 5009-18.
Journal code: ECW. ISSN: 0950-1991.

L11 ANSWER 4 OF 7 CAPLUS COPYRIGHT 1999 ACS
TI A novel developmental regulatory motif required for stage-specific
activation of the .epsilon.-globin gene and nuclear factor binding in
embryonic erythroid cells
AU Trepicchio, William L.; Dyer, Michael A.; **Baron, Margaret H.**
SO Mol. Cell. Biol. (1994), 14(6), 3763-71
CODEN: MCEBD4; ISSN: 0270-7306

L11 ANSWER 5 OF 7 CAPLUS COPYRIGHT 1999 ACS
TI Positive regulators of the lineage-specific transcription factor GATA-1
in
differentiating erythroid cells
AU **Baron, Margaret H.; Farrington, Sarah M.**
SO Mol. Cell. Biol. (1994), 14(5), 3108-14
CODEN: MCEBD4; ISSN: 0270-7306

L11 ANSWER 6 OF 7 CAPLUS COPYRIGHT 1999 ACS
TI Developmental regulation of the human embryonic .beta.-like globin gene
is
mediated by synergistic interactions among multiple tissue- and
stage-specific elements
AU Trepicchio, William L.; Dyer, Michael A.; **Baron, Margaret H.**
SO Mol. Cell. Biol. (1993), 13(12), 7457-68
CODEN: MCEBD4; ISSN: 0270-7306

L11 ANSWER 7 OF 7 CAPLUS COPYRIGHT 1999 ACS
TI Reprogramming of globin gene expression in interspecific heterokaryons
AU **Baron, Margaret H.; Maniatis, Tom**
SO UCLA Symp. Mol. Cell. Biol., New Ser. (1987), 51(Mol. Approaches Dev.
Biol.), 469-76
CODEN: USMBD6; ISSN: 0735-9543

L1 ANSWER 1 OF 2 INPADOC COPYRIGHT 1999 EPO
AN 28952038 INPADOC UW 9909 UP 990313 EW 9909 ED 990313
TI METHODS FOR MODULATING HEMATOPOIESIS AND VASCULAR GROWTH.
IN BARON, MARGARET, H.; FARRINGTON, SARAH, M.; BELAOUSSOFF, MARIA
INS BARON MARGARET H; FARRINGTON SARAH M; BELAOUSSOFF MARIA
PA THE PRESIDENTS AND FELLOWS OF HARVARD COLLEGE
PAS PRESIDENTS AND FELLOWS OF HARV
PAA US
LA English
TL English; French
DT Patent
PIT WO A3 SUBSEQUENT PUBL. OF THE INT. SEARCH REPORT
PI WO 9835020 A3 990114 300000
DS W CA; W JP
RW AT; RW BE; RW CH; RW DE; RW DK; RW ES; RW FI; RW FR; RW GB; RW GR; RW
IE; RW IT; RW LU; RW MC; RW NL; RW PT; RW SE
AI WO 98-US2633 A 980210
PRAI US 97-37513 P 970210 EWPR 9835 EDPR 980905
US 97-49763 P 970616 EWPR 9835 EDPR 980905

VEGF + TKE TER

45,585,087

5,585,237

5,565,321